ACUTE TOXICITY SUMMARY

SULFUR DIOXIDE

(sulfur oxide; sulfurous anhydride; sulfurous oxide)

CAS Registry Number: 7446-09-5

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**660 μg/m³**
Critical effect(s)	impairment of airway function, especially in asthmatics
Hazard Index target(s)	Respiratory system

II. Physical and Chemical Properties (from HSDB, 1994 except as noted)

Description	colorless gas
Molecular formula	SO_2
Molecular weight	64.1
Density	2.62 g/L @ 25°C
Boiling point	-10°C
Melting point	-72.7°C
Vapor pressure	2432 mm Hg @ 20°C
Flashpoint	unknown
Explosive limits	unknown
Solubility	soluble in water, ethanol, chloroform, ether, acetic acid
Odor threshold	0.62 - 1.2 ppm (Ryazanov, 1961)
Odor description	pungent, irritating odor
Metabolites	sulfate (SO_4^{2-}) salts
Conversion factor	1 ppm = 2.62 mg/m³ @ 25°C

III. Major Uses or Sources

Sulfur dioxide is a product of combustion from coal and other fuel burning. In addition, there are many natural sources of atmospheric SO_2, including volcanoes and marine and terrestrial biogenic emissions (CARB, 1983). The decay of biologic materials containing sulfur results in the release of reduced sulfur compounds which are oxidized to SO_2 and other sulfur oxides (CARB, 1983). Anthropogenic sources of sulfur dioxide in ambient air include oil refineries, power plants and automobiles.

IV. Acute Toxicity to Humans

A thorough review of the scientific and epidemiological literature regarding the acute toxicity of sulfur dioxide (SO_2) to animals and humans can be found in the Recommendation for the one-hour Ambient Air Quality Standard for sulfur dioxide (OEHHA, 1994). Several of the most sensitive studies considered in the development of the California Ambient Air Quality Standard (CARB, 1983) for SO_2 are described below.

Increased airway resistance (SRaw) in asthmatics following exposure to SO_2 has been frequently reported. Horstman *et al*. (1986) exposed 27 adults with mild asthma to 0, 0.25, 0.5, 1.0, and 2.0 ppm (0, 0.66, 1.31, 2.62, and 5.24 mg/m³) SO_2 for 10 minutes of moderate exercise. The exposure concentrations required for a 100% increase in SRaw varied considerably in the study group, from less than 0.5 ppm (1.31 mg/m³) to greater than 2.0 ppm (5.24 mg/m³). The median concentration to which these subjects responded with a 100% increase in SRaw was 0.75 ppm (1.97 mg/m³).

Linn *et al*. (1983) reported that moderate to severe asthmatics with a ventilation rate of approximately 48 L/minute exhibited increased SRaw of 120% when exposed to 0.4 ppm (1.05 mg/m³) SO_2 for 5 minutes.

A study on the acute effects of SO_2 on SRaw was conducted by Linn *et al*. (1987). Included in this study were mild, moderate, and severe asthmatics, atopic individuals, and normal subjects. These subjects were exposed to 0, 0.2, 0.4, or 0.6 ppm (0, 0.52, 1.05, or 2.1 mg/m³) SO_2 for 1 hour. Analysis of the Linn data by OEHHA scientists showed that statistically significant increases in SRaw and respiratory symptoms were present in atopic individuals exposed to 0.6 ppm for 15-55 minutes, and in moderate to severe asthmatic individuals at 0.4 ppm after 55 minutes. Mild asthmatics were the only group that showed a significant increase in SRaw and respiratory symptoms at 0.2 ppm. OEHHA staff also analyzed data from the most sensitive 30 percent of the subjects studied by Linn *et al*. (1987), and found that asthmatics, atopics, and normal subjects all exhibited statistically significantly increased SRaw after exposure to 0.2 ppm. However, at this concentration, the changes in SRaw were not considered clinically significant, since they were not accompanied by respiratory symptoms. Of these groups, asthmatics were the most sensitive to the effects of SO_2 on SRaw.

Male volunteers with mild asthma were exposed to 0.0, 0.25, 0.5, or 1.0 ppm SO_2 for 75 minutes (Roger *et al*., 1985). Each exposure included three 10 minute moderate treadmill exercise periods. Specific airway resistance was not significantly increased after exercise with 0.25 ppm SO_2 compared to clean air exposure, but was significantly increased with 0.5 and 1.0 ppm SO_2.

A study by Bethel *et al*. (1985) showed that asthmatics exposed for 15 minutes to 0.25 ppm SO_2 had significantly increased SRaw. However, exposure in this study was via mouthpiece and may have resulted in a greater dose than similar concentrations in chamber exposures. Furthermore, the results of Bethel *et al*. could not be reproduced at higher exposures and workloads.

Fourteen healthy non-smokers (7 men and 7 women), between 20 and 46 years old, were exposed for 30 minutes to filtered air while free breathing and to 2.0 ppm SO_2 with either free breathing, forced oral, or forced nasal breathing with continuous exercise (Bedi and Horvath, 1989). Lack of changes in pulmonary function tests including airway resistance indicated that 2.0 ppm SO_2 did not adversely affect normal subjects.

Predisposing Conditions for Sulfur Dioxide Toxicity

Medical: Asthmatics are more sensitive to the irritant effects of SO_2 than non-asthmatics, especially when exercising or when in cold, dry air (Koenig *et al*., 1982; Bethel *et al*., 1984). Some allergic or atopic individuals and people with Reactive Airways Disease Syndrome (RADS; acute, irritant-induced asthma) may also be more sensitive to SO_2 irritation (Linn *et al*., 1987).

Chemical: Co-exposures to other irritants such as sulfuric acid, nitrogen dioxide, and ozone may potentiate the irritant effects of SO_2 on pulmonary function in asthmatics (OEHHA, 1994). In animals, co-exposure to ozone has been shown to increase the irritancy of SO_2 and to increase airway responsiveness (Amdur *et al*., 1978).

V. Acute Toxicity to Laboratory Animals

Due to the abundance of clinical data collected using human asthmatics, animal data were not used as the basis for the 1-hour Ambient Air Quality Standard for SO_2.

VI. Reproductive or Developmental Toxicity

Reports of reproductive effects in the human workplace have involved mixed exposures, and are not definitive. Some data in rats indicate that SO_2 affects the estrous cycle, increases the incidence of fetal resorptions, and impairs fetal development at concentrations as low as 4.97 mg/m³ (Reprotext, 1993).

VII. Derivation of Acute Toxicity Exposure Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 660 µg/m³

Study	multiple studies as cited in OEHHA, 1994
Study population	multiple studies of healthy, asthmatic and atopic volunteers
Exposure method	controlled inhalation exposures with or without exercise
Critical effects	adverse respiratory effects, bronchoconstriction
LOAEL	0.4 ppm for 5 minutes (Linn *et al*., 1983)
	0.4 ppm for 60 minutes (Linn *et al*., 1987)
	0.5 ppm for 75 minutes (Roger *et al*., 1985)
NOAEL	0.25 ppm for 75 minutes (Roger *et al*., 1985)

	0.2 ppm for 60 minutes (Linn *et al.*, 1987)
Exposure duration	varied
Equivalent 1 hour concentration	0.25 ppm (consensus value from multiple studies)
LOAEL uncertainty factor	1
Interspecies uncertainty factor	1
Intraspecies uncertainty factor	1
Cumulative uncertainty factor	1
Reference Exposure Level	0.25 ppm (250 ppb; 0.66 mg/m³; 660 µg/m³) (California Ambient Air Quality Standard)

After reviewing several studies on controlled human data on acute exposures of normal, asthmatic, and atopic individuals to low concentrations of SO_2 (0.25 - 2.0 ppm), OEHHA staff concluded that exposure to 0.25 ppm, the California Ambient Air Quality Standard (CAAQS) for SO_2, would not result in discomforting respiratory effects in sensitive individuals for a period of 1-hour. The CAAQS for SO_2 aims to protect sensitive individuals (i.e., exercising asthmatics) from lower respiratory effects of acute exposure. The procedures used to derive the CAAQS were not identical to those in this report. However, based on a thorough review of the literature, OEHHA staff concluded that an exposure concentration of 0.25 ppm SO_2 for 1 hour is comparable to a NOAEL in sensitive individuals. This level is felt to protect asthmatic individuals because adverse effects are consistently observed only at higher concentrations under conditions of moderate exercise (ventilation rates of > 40 L/minute) and there is an inconsistency in response to SO_2 exposure at lower concentrations.

Level Protective Against Severe Adverse Effects

No recommendation is made due to the limitations of the database.

Asthmatics exposed via a mouthpiece to 5 ppm SO_2 for 10 minutes required bronchodilator therapy because of bronchoconstriction resulting from the exposure (Sheppard *et al*., 1980). The Sheppard *et al*. (1980) study was a mouthpiece study, and therefore most likely resulted in a greater inhaled dose of SO_2 than in chamber studies. The AIHA (1992) developed an ERPG-2 of 3 ppm (7.86 mg/m³) and stated that exposures above 3 ppm are likely to cause bronchoconstriction of varying severity in a significant portion of the population. This could impair the ability to take protective action. There is therefore no margin of safety included for protection of these individuals from severe effects, a serious shortcoming.

Level Protective Against Life-threatening Effects

No recommendation is made due to the limitations of the database.

Many reports show that asthmatics exposed to SO_2 at low concentrations (0.37-5 ppm) exhibit bronchoconstriction (Amdur, 1974; Bell *et al*., 1977; Bethel *et al*., 1983, 1984; Koenig *et al*., 1980, 1982; Linn *et al*., 1977, 1983, 1984; Sheppard *et al*., 1980, 1981). In its selection of an ERPG-3 for SO_2 of 15 ppm (39.3 mg/m³), the AIHA (1992) acknowledges that the bronchoconstriction observed in asthmatics could be potentially life-threatening, but does not include specific information about the adoption of the 15 ppm value. The ERPG-3 is based on estimation of lethality in asthmatics exposed to SO_2 for 1-hour. Although the ERPG document correctly considers asthmatics as a sensitive subpopulation for this level, the specific rationale used to develop a margin of safety for the ERPG-3 is not presented, a serious shortcoming.

NIOSH (1995) lists an IDLH for sulfur dioxide of 100 ppm. It is based on the statement by AIHA (1955) that 50 to 100 ppm is considered the maximum concentration for exposures of 0.5 to 1 hour (Henderson and Haggard, 1943).

VIII. References

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